

Prostaglandin pathway regulation of self-renewal in hematopoietic and leukemia stem cells

Grant Award Details

Prostaglandin pathway regulation of self-renewal in hematopoietic and leukemia stem cells

Grant Type: Basic Biology IV

Grant Number: RB4-06036

Project Objective: The overall objectives are to investigate the molecular mechanisms that sustain leukemia stem cells, with the ultimate goal of defining novel cancer stem cell pathways, markers and therapeutic targets. In particular, aberrations in the MLL/Hox/Meis pathway will be explored to elucidate their effects on self-renewal of leukemic stem cells in a subset of AML.

Investigator:

Name:	Michael Cleary
Institution:	Stanford University
Type:	PI

Disease Focus: Blood Cancer, Cancer

Human Stem Cell Use: Adult Stem Cell, Cancer Stem Cell

Award Value: \$1,244,455

Status: Closed

Progress Reports

Reporting Period: Year 1

[View Report](#)

Reporting Period: Year 2

[View Report](#)

Reporting Period: Year 3/NCE

[View Report](#)

Grant Application Details

Application Title: Prostaglandin pathway regulation of self-renewal in hematopoietic and leukemia stem cells

Public Abstract: Leukemias are cancers of the blood cells that result from corruption of the normal controls that regulate blood-forming stem cells. They are serious causes of illness and death, and are particularly devastating in children and the elderly. Despite substantial advances in treatment of leukemia, a significant proportion of cases are unresponsive to current therapy. Since more aggressive chemotherapy regimens provide only marginal improvements in therapeutic efficacy, we have reached a point of diminishing returns using currently available drugs. Thus, there is an urgent need for more targeted, less toxic, and more effective treatments. To this end, our studies focus on defining the defects that corrupt the normal growth controls on blood stem cells. The proposed studies build on our discovery of a key enzyme with an unexpected causative role in leukemia. We propose to further characterize its function using various proteomic approaches, and employ a cross-species comparative approach to identify additional pathways unique to cancer stem cell function. The proposed characterization of crucial growth controls that go awry in blood stem cells to cause leukemia will identify new drug targets for more effective and less toxic treatments against these devastating, life-threatening diseases.

Statement of Benefit to California: Leukemias are cancers of the blood cells that cause serious illness and death in children and adults. They result from corruption of the normal controls that regulate blood-forming stem cells. Despite many attempts to improve treatments with new drug combinations, this approach has reached a point of diminishing returns since intensified chemotherapies contribute only marginal improvement in outcome and are associated with increasing toxicity. The proposed characterization of crucial growth controls that go awry in blood stem cells to cause leukemia will identify new drug targets for more effective and less toxic treatments against these devastating, life-threatening diseases.

Source URL: <https://www.cirm.ca.gov/our-progress/awards/prostaglandin-pathway-regulation-self-renewal-hematopoietic-and-leukemia-stem>